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Scientific evidence on the links between periodontal diseases and diabetes: consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the international Diabetes Federation (IDF) and the European Federation of Periodontology.

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Key words: periodontal disease, periodontitis, diabetes mellitus, type 2 diabetes, type 1 diabetes, gestational diabetes, association, HbA1c, complications, mechanisms, intervention, incident, chronic kidney disease, mortality, retinopathy, nephropathy.

Conflict of interest and source of funding statement

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Abstract

Background: Diabetes and periodontitis are chronic non-communicable diseases that are independently associated with mortality and have a bi-directional relationship, whereby each disease is associated with the other disease leading to poorer disease status. The relationship between periodontitis and diabetes was defined by an international workshop in 2012 and guidelines were produced. Since then, substantial new evidence has emerged for their inter-relationship.

Aims: To update the evidence for epidemiological and mechanistic associations between periodontitis and diabetes and re-examine the impact of effective periodontal therapy upon metabolic control (HbA1C).

Epidemiology: There is strong evidence that people with periodontitis have elevated risk for dysglycemia and insulin resistance. Cohort studies among people with diabetes demonstrate significantly higher HbA1C levels in periodontitis patients (vs. periodontally healthy), but there is insufficient data among people with type 1 diabetes. Periodontitis is also associated with an increased risk of incident type 2 diabetes. The co-morbid presence of periodontitis with diabetes imparts a higher risk of microvascular and macrovascular (nephropathy) complications and is associated with significantly higher all-cause and cardiovascular mortality.

Mechanisms: Mechanistic links between periodontitis and diabetes involve elevations in interleukin (IL) 1- β , tumor necrosis factor- α , IL-6, receptor activator of nuclear factor-kappa B ligand/osteoprotegerin ratio, oxidative stress and toll-like receptor (TLR)2/4 expression.

Interventions: periodontal therapy is safe and effective in people with diabetes and it is associated with reductions in HbA1C of 0.27-0.48% after 3-months, although studies involving longer-term follow up are inconclusive.

Conclusions: Based on the most contemporary literature, the European Federation of Periodontology (EFP) and the International Diabetes Federation (IDF) report consensus guidelines for physicians, oral health care professionals and patients in order to improve rates of diagnosis for diabetes and pre-diabetes, and also to improve periodontal outcomes in people with diabetes.

Clinical Relevance

Scientific Rationale for Study

Periodontitis and diabetes are chronic non-communicable diseases that impact upon the course and outcome of each other and also appear to interact in a manner that increases the risk of all-cause and cardiovascular mortality. This joint workshop between the European Federation of Periodontology (EFP) and the International Diabetes Federation (IDF) updated the evidence from the international EFP/AAP workshop in 2012 and developed consensus statements about the relationship between these two important diseases.

Principal Findings

Poor glycaemic control in diabetes is associated with poorer periodontal status and outcomes. Periodontitis is associated with disglycaemia and increased insulin resistance in people with diabetes, as well as increased risk for incident diabetes and diabetes complications, including mortality. Periodontal therapy improves serum HbA1C levels and is safe to perform, though there is limited evidence for adjunctive therapies.

Practical Implications

The oral healthcare team have a role to play in identifying both pre-diabetes and undiagnosed diabetes mellitus and physicians need to be aware of periodontal diseases and their implications for glycaemic control and complications in people with diabetes. Guidelines are documented for physicians, oral healthcare workers, patients and the public.

Introduction

Periodontitis is a ubiquitous chronic inflammatory disease, initiated by the accumulation of a pathogenic dental plaque biofilm above and below the gingival (gum) margin, and within which microbial dysbiosis leads to a chronic non-resolving and destructive inflammatory response (Meyle & Chapple 2015, Jepsen et al. 2017). It has a prevalence of 45-50% in adults in its mildest form rising to over 60% in people over 65 years of age (64% - Eke et al. 2012, 60% - White et al. 2012). Severe periodontitis is estimated to affect 11.2% of the global adult population (Kassebaum et al. 2014) and is a major cause of tooth loss, nutritional compromise, altered speech, low self-esteem and a poorer overall quality of life (Al-Harthi et al. 2013, Buset et al. 2016). Severe periodontitis is also independently associated with mortality in several different populations (Garcia et al. 1998, Linden et al. 2012, Soikkonen et al. 2000, Söder et al. 2007). When present as a co-morbidity in patients with chronic kidney disease (CKD), it is associated with a 41% increase in 10-year all-cause mortality rates and a 22% elevation in 10-year cardiovascular mortality rates (verses increases of 36% and 16% in CKD patients without periodontitis) (Sharma et al. 2016). The co-morbid presence of periodontitis and diabetes in CKD patients is reported to elevate 10-year all-cause mortality risk by 23% and cardiovascular mortality risk by 16% in CKD patients, with the additional impact on survival when periodontitis is present being equivalent to the impact of diabetes as a co-morbid risk factor in CKD (Sharma et al. 2016). Diabetes is global epidemic disease. It is estimated there are now more than half a million children aged 14 and under living with type 1 diabetes. It is also estimated that there are already 415 million adults aged 20-79 with diabetes worldwide, including 193 million who are undiagnosed. A further 318 million adults are estimated to have impaired glucose tolerance, which puts them at high risk of developing the disease. By the end of 2015, diabetes caused 5.0 million deaths and had a cost between USD 673 billion and USD 1,197 billion in healthcare spending. If this rise is not halted, by 2040 there will be 642 million people living with the disease (International Diabetes Federation 2015).

The significant and independent association between periodontitis and chronic non-communicable diseases of ageing is widely reported in the literature. Such data provided the impetus for an international workshop in 2012, where consensus statements for periodontitis and atherogenic cardiovascular disease (Tonetti & Van Dyke 2013), periodontitis and diabetes (Chapple & Genco 2013), and periodontitis and adverse

pregnancy outcomes (Sanz & Kornman 2013) were developed, based upon 10 systematic reviews addressing epidemiology, mechanisms of association and periodontal intervention studies. A common theme that emerged was the impact of periodontal bacteremia/endotoxemia following daily activities such as eating and tooth brushing upon low-grade systemic inflammation, via acute-phase (C-reactive protein, CRP) and neutrophil oxidative stress responses.

The evidence base for independent associations between periodontitis and type 2 diabetes is long established, with a dual directionality of influence reported (Taylor et al. 2001). In the diabetes-periodontitis direction, hyperglycemia is associated with an increased risk and severity of periodontitis (Cianciola et al. 1982, Lalla et al. 2006, Emrich et al. 1991, Taylor et al. 1998) and poorer periodontal outcomes following periodontal therapy (Mealey 2006). Indeed, the addition of periodontal measures, such as suppuration and indicators of periodontal disease severity and extent to risk assessment methods for diabetes significantly improves screening diagnostic rates. In a United States of America (USA)-based study, screening for diabetes in the dental setting was effective in identifying both pre-diabetes and diabetes (Albert et al. 2012) and early detection led to the instigation of cost-effective lifestyle change measures that resulted in a significant proportion of patients moving from pre-diabetes to normo-glycaemia during the trial period. In the United Kingdom, the National Institute of Clinical Excellence has suggested that other health care professionals other than physicians, including dentists, should be screening for diabetes ([https://www.nice.org.uk/guidance/ph38/chapter/1-Recommendations# recommendation-1-risk-assessment](https://www.nice.org.uk/guidance/ph38/chapter/1-Recommendations#recommendation-1-risk-assessment)).

In the periodontitis-diabetes direction, the 2012 workshop concluded that severe periodontitis was associated with significantly elevated serum levels of HbA1C in people without diabetes (glycemia) and in those with diabetes (hyperglycemia), and there appeared to be a direct relationship between the severity of the periodontitis and cardio-renal complications of diabetes (Borgnakke et al. 2013). Severe periodontitis is also associated with dyslipidaemia and elevations in oxidative stress markers in the serum of people with type 2 diabetes (Allen et al. 2011). Emerging evidence also indicates that people with severe periodontitis have an increased risk of developing type 2 diabetes (Saito et al 2004, Demmer et al 2008, Morita et al 2012). Finally, in the systematic review aimed at

addressing the impact of periodontal treatment upon serum HbA1C levels, a mean reduction in HbA1C of 0.36% [95% confidence interval (CI) 0.19, 0.54] was demonstrated at 3-months (Engebretson & Kocher 2013), a result that was consistent with previous meta-analyses.

Given the continued global research effort into the periodontitis-diabetes paradigm, this joint international workshop between the European Federation of Periodontology (EFP) and the International Diabetes Federation (IDF), and involving 15 experts from Europe, the USA and South Asia, aimed at developing consensus statements based upon the evidence for epidemiological associations, pathogenic mechanisms, and intervention studies of periodontal treatment and its impact upon diabetes outcomes. Evidence from 2012 in these domains was updated from the systematic reviews of 2012 and the resulting consensus statements and guidelines (Chapple & Genco 2013), were also updated to inform the development of new guidelines for physicians and their patients, and oral healthcare workers and their patients.

The objective of this workshop was to update the evidence base on the bidirectional association between periodontitis and type 2 diabetes and provide recommendations for the global multidisciplinary team caring for people with diabetes and periodontitis.

Epidemiologic evidence on the effect of periodontitis on diabetes

Among people without diabetes, is periodontitis associated with elevated glucose levels?

There is strong evidence for an association between periodontitis and glycemic status, expressed as HbA1C, fasting blood glucose levels and/or OGTT in people who have no manifest diabetes. People with periodontitis have a higher level of HbA1C [weighted mean (WM) of 5.64%; 95% CI, 5.54-5.74%], when compared to people with better periodontal health (WM 5.31 %; 95% CI, 5.18-5.44%) where the WM difference in HbA1C is 0.29% (95% CI, 0.20-0.37%, $p < 0.01$) (Graziani et al 2017).

Among people with type 2 diabetes, is periodontitis associated with poorer glycemic control?

In three cohort studies (N=1252), including one with a large sample (N=1021), periodontitis was significantly associated with poorer glycemic control as measured by HbA1C

(7.4% vs. 7.0%). This risk was more marked in those patients with poorer HbA1C at baseline. By contrast, 4 cross-sectional (N=1076), 1 case-control (N=60) and 1 cohort study (N=42) did not report a significant difference of HbA1C levels when comparing people with different levels of periodontal status. Some studies, however, identified higher insulin resistance (HOMA-IR levels) in people with periodontitis (Graziani et al 2017).

Among people with type 1 diabetes, is periodontitis associated with poorer glycemic control?

There is insufficient data (one clinical study) within the current literature to answer this question conclusively.

Among people with diabetes, is periodontitis associated with more diabetes complications?

Diabetes complications studied in relation with periodontitis are: retinopathy (background and proliferative), nephropathy (proteinuria and end-stage renal disease), neuropathic foot ulceration, various cardiovascular diseases and mortality. The overall synthesis is drawn from 13 studies involving 34,149 subjects.

Retinopathy is significantly associated with periodontitis after adjusting for other confounding factors [5 studies; odds ratio (OR) 1.2-2.8]. Emerging evidence indicates that the severity of periodontitis correlates significantly with the severity of retinopathy.

There is evidence from three studies that people with periodontitis and with either type 1 or type 2 diabetes have significantly more renal complications. In one large study, chronic kidney disease (CKD) was associated with significantly more all-cause and cardiovascular mortality when periodontitis and diabetes were present at the same time as the CKD, than when either were present as individual and independent comorbidities in CKD (Sharma et al. 2016).

A significant association of neuropathic foot ulcerations in patients with severe periodontitis compared to healthy controls was demonstrated in one study (OR 6.6).

Cardiovascular complications (cardiovascular mortality, coronary heart disease or cerebrovascular events, sub-clinical heart disease) have been significantly associated with type 2 diabetes patients suffering from periodontitis [hazard ratios (HR) 1.1 –

1.3] (OR 2.6). Overall mortality is significantly elevated in patients with type 2 patients with co-morbid periodontitis (HR 3.5-4.5).

In summary, the majority of studies report a higher association/risk between worse periodontal conditions and diabetes complications.

Do people with periodontitis have a greater risk of developing type 2 diabetes than those with better periodontal health?

Overall, evidence from 6 studies representing populations of USA, Japan and Taiwan with a total sample of 77,716 participants consistently demonstrated that periodontitis patients exhibit a higher chance of developing pre-diabetes and diabetes (adjusted HR 1.29; 95% CI, 1.11-1.46, $p < 0.0001$) (Graziani et al 2017).

Do women with gestational diabetes and periodontitis have poorer glycaemic control than those with better periodontal health?

There is insufficient data addressing the question of whether periodontitis impairs glycemic control in gestational diabetes.

Do pregnant women with periodontitis have a higher incidence of gestational diabetes than those with better periodontal health?

There are no studies assessing whether pregnant women with periodontitis have an altered risk of developing gestational diabetes. However, two studies have shown a significant association.

Mechanistic Links between Periodontal Diseases and Diabetes

Is the periodontal microbiota affected by diabetes status?

Traditional approaches to analyzing the periodontal microbiota did not report consistent differences between people with and without diabetes. Emerging evidence from small-scale molecular periodontal microbiome studies do indicate an association between altered glucose metabolism in pre-diabetes and diabetes and changes in the periodontal microbiome. Currently, there is no data supporting a causal relationship between the periodontal microbiome and the presence of diabetes. The majority of studies address type 2 diabetes (Polak & Shapira et al 2017).

In people with diabetes, what is the role of cytokines and other inflammatory mediators in the pathogenesis of periodontitis?

There is evidence from clinical studies to support the contention that elevated levels of pro-inflammatory mediators in poorly controlled diabetes [interleukin (IL) 1- β , tumoral necrosis factor (TNF)- α , IL-6, receptor activator of nuclear factor-kappa B ligand/osteoprotegerin ratio and oxidative stress] within the gingival tissues of people (or animal models) with diabetes play a role in the observed increased periodontal destruction. This is supported by studies using cell cultures exposed to high glucose levels (Polak & Shapira et al 2017).

Which mechanisms affect the control of diabetes and its complication in people with periodontitis?

There is a moderate level of evidence to support certain biological mechanisms mediating the effect of periodontitis on the control of diabetes. There is evidence for reduced beta-cell function, elevated oxidative stress and dyslipidaemia in people with type 2 diabetes and periodontitis relative to diabetes alone. Most studies demonstrate that circulating pro-inflammatory mediators are elevated in people with diabetes and periodontitis, particularly TNF- α , CRP and mediators of oxidative stress. These pro-inflammatory mediators may affect the control of diabetes. Unfortunately, there is no data from animal studies to support this possibility.

There is no direct evidence for specific mechanisms arising from periodontitis impacting upon the complications of diabetes. However, indirect evidence exists for common mechanistic pathways (oxidative stress pathways, dyslipidaemia, elevated CRP, endothelial dysfunction) that may act synergistically in worsening cardiovascular complications in diabetes.

Is there mechanistic evidence that improving the control of diabetes results in improved periodontal status?

There is mechanistic evidence that improving the control of diabetes reduces oxidative stress, improves lipid profiles and reduces circulating cytokine levels, however, there are no studies relating such biological changes to improvements in periodontal status.

Is there mechanistic evidence that improving periodontal health results in improved metabolic control and/or complications of diabetes?

There is evidence from several controlled human studies, which shows that successful periodontal treatment reduces circulating levels of CRP and TNF- α in people with diabetes (Polak & Shapira et al 2017). There have been no studies addressing the impact of successful long-term periodontal therapy upon the mechanisms involved in diabetes complications.

Results of Intervention Studies

Is it possible to manage periodontitis in people with diabetes?

Current evidence indicates that in people with diabetes, periodontal therapy accompanied by effective home care is both safe and effective. Clinical periodontal parameters and local inflammatory measures improve following standard non-surgical therapy even in people with poorly controlled diabetes. The benefits of adjunctive treatments (e.g. antimicrobial, surgical) needs further investigation, because the majority of previous studies intervened using professional mechanical debridement without the use of adjunctive treatments.

Is periodontal treatment effective in improving glycaemic control in people with type 2 diabetes?

After the previous systematic review by Engebretson & Kocher (2013), at least 7 randomised clinical trial (RCTs) have been published including a total of 912 patients from 3 countries (India, Malaysia, USA) (Madianos & Koromantzos 2017). Data from 4 recent systematic reviews with meta-analyses (published between 2014 and 2017, with substantial but not complete overlap of existing RCTs), have provided consistent evidence for a clinically meaningful and statistically significant reduction of HbA1C levels in people with type 2 diabetes. The magnitude of reported HbA1C reductions from these meta-analyses ranges from 0.27- 0.48% at 3 - 4 months following periodontal therapy.

There is insufficient data to demonstrate that this effect is maintained at 6 months.

It should be noted that the reported improvements in HbA1C levels after periodontal therapy (currently estimated at 0.27 to 0.48%) are in agreement with the magnitude of increase in HbA1C attributed to periodontitis in type 2 diabetics 0.29 % (95% CI, 0.20-0.37 %) (Madianos & Koromantzos 2017). The increase in glycated hemoglobin due to periodontitis is similar in magnitude to the observed improvement once periodontitis is treated.

The magnitude of short-term HbA1C reductions obtained following periodontal interventions is similar to that often achieved by adding a second medication to a pharmacological regimen. If such reductions following periodontal therapy can be sustained over the longer term, then this may contribute to reduced diabetes-associated morbidity and mortality.

Is periodontal treatment effective in improving glycaemic control in people with type 1 diabetes?

There is insufficient evidence about the effect of periodontal therapy on HbA1C reduction in people with type 1 diabetes due to paucity of studies. The biological plausibility linking periodontal therapy to improved glycaemic control among people with type 1 diabetes is unclear and requires further exploration.

Do adjunctive antibiotics confer additional benefits and enhance glycemic control?

The adjunctive use of antibiotics does not enhance HbA1C reduction beyond scaling and root planing alone among people with type 2 diabetes. There is insufficient data for the adjunctive benefit of antibiotics among people with type 1 diabetes.

What is the specific level of periodontal resolution following periodontal therapy that is associated with improvements in diabetes outcomes?

While periodontal therapies result in reduction in HbA1C levels, people with diabetes, on average benefit from periodontal therapy. At present, no specific threshold of periodontal disease resolution has been identified as necessary to realize HbA1C reduction. Thresholds of improvement in clinical periodontal parameters necessary to confer meaningful reductions of HbA1C levels should be explored in future RCTs. Future meta-analyses could use meta-regression approaches to inform this question.

Guidelines

Guidelines for physicians and other medical health professions for use in Diabetes Practice

Because of the increased risk for developing periodontitis in patients with diabetes and the negative impact of periodontitis on diabetes control and complications, the following recommendations are made:

- Oral health education should be provided to all patients with diabetes as part of their overall educational program.

- Patients with all forms of diabetes mellitus should be told that periodontal disease risk is increased, and if untreated the periodontitis has a negative impact on metabolic control and may also increase the risk of complications of their diabetes such as cardiovascular and kidney disease.
- Patients should be advised that successful periodontal therapy may have a positive impact upon their metabolic control and diabetes complications.
- For people with diabetes, physicians should ask about a prior diagnosis of periodontal disease. If a positive diagnosis has been made, the physician should seek to ascertain that periodontal care and maintenance are being provided.
- Investigating the presence of periodontal disease should be an integral part of a diabetes care visit. People with diabetes should be asked about any signs and symptoms of periodontitis, including bleeding gums during brushing or eating, loose teeth, spacing or spreading of the teeth, oral malodor, and/or abscesses in the gums or gingival suppuration.
 - If a positive history is elicited then a prompt periodontal evaluation should be recommended before their scheduled annual check-up.
 - In the case of a negative history, people with diabetes should be advised to check for the above symptoms and if a positive sign appears they should visit their dentist.
- For all people with newly diagnosed diabetes mellitus, referral for a periodontal examination should occur as part of their ongoing management of diabetes. Even if no periodontitis is diagnosed initially, annual periodontal review is recommended.
- For children and adolescents diagnosed with diabetes, annual oral screening is recommended through referral to a dental professional.
- Patients with diabetes who have extensive tooth loss should be encouraged to pursue dental rehabilitation to restore adequate mastication for proper nutrition.

- Patients with diabetes should be advised that other oral conditions such as dry mouth and burning mouth may occur, and if so, they should seek advice from their dental practitioner. Also, patients with diabetes are at increased risk of oral fungal infections and experience poorer wound healing than those who do not have diabetes.
- The physician should liaise with the dentist over diabetes management prior to the oral intervention and/or surgery in order to avoid hypoglycaemia and to consider its potential impact on the patient's ability to eat.

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ⁱ *The above guidelines also apply to people with pre-diabetes and the metabolic syndrome.*
ⁱⁱ *These guidelines are modified from (Chapple & Genco 2013) and also draw upon http://www.aemmedi.it/files/Linee-guida_Raccomandazioni/2015/Diabete%20e%20Parodontite_AMD_SID_SiDP.pdf*

Guidelines for patients with diabetes at the physician's practice/office

Why should I have my gums checked?

If your physician has told you that you have diabetes, you should make an appointment with a dentist to have your mouth and gums checked. This is because people with diabetes have a higher chance of getting gum disease. Gum disease can lead to tooth loss and may make your diabetes harder to control. The earlier you seek help the better the outcome will be.

What should I look for that may tell me I have problems with my gums?

You may have gum disease if you have ever noticed:

- Red or swollen gums;
- Bleeding from your gums or blood in the sink after you brush your teeth;
- Foul taste;
- Longer looking teeth;
- Loose teeth;
- Increasing spaces between your teeth;

- Calculus (tartar) on your teeth.

If you have noticed any of these problems, it is important to see a dentist as soon as possible.

Can I have gum disease without these signs being present?

Gum disease may also be present and get worse with no apparent signs to you, especially if you smoke, so even if you do not think you have gum disease now, you should still have annual dental check-ups as part of managing your diabetes. Your dentist will be able to pick up early signs of gum disease.

What can I do to prevent gum disease?

You need to clean your teeth and gums twice daily at home for a minimum of two minutes. Also, cleaning between your teeth daily is important and your oral health professional will show you how to do this. You should visit a dentist as soon as possible for a diagnosis and advice on what you need to do. It is important to keep your mouth as healthy as possible with regular dental care, according to the recommendations of your oral health professional.

What other problems with my mouth should I be looking for?

If you have diabetes, you may also suffer from dry mouth, burning mouth, or poor healing of mouth wounds.

Guidelines for oral health professionals for use in dental practice/office for people with diabetes mellitus

- People with diabetes should be advised that they have an increased risk for gingivitis and periodontitis. They should also be told that if they suffer from periodontitis, their glycaemic control may be more difficult to achieve, and they are at higher risk for other complications such as eye disease, kidney and cardiovascular diseases.
- Collect a careful history to highlight the type of diabetes, duration of the disease, the presence of any complications, diabetes therapy and concomitant therapies, remembering that most people with diabetes are also being treated

with anticoagulant/antiplatelet drugs, antihypertensive drugs or lipid-lowering medications.

- Ask the patient how well controlled their diabetes is and when they last had their blood glucose levels checked. Request that patients bring a copy of their last HbA1C result, or that they report their latest results.
- Oral health education should be provided to all patients with diabetes. This should include individualised advice on relevant risk factors and a tailored oral hygiene regime, including twice daily brushing, interdental cleaning and in some cases the use of adjunctive chemical plaque control may be appropriate.
- People presenting with a diagnosis of any form of diabetes mellitus should receive a thorough oral examination, which includes a comprehensive periodontal evaluation, to include full mouth pocket chart and bleeding scores if indicated by periodontal screening.
- If no periodontitis is diagnosed initially, patients with diabetes should be placed on a preventive care regime and monitored regularly for periodontal changes.
- People with diabetes presenting with any acute oral/periodontal infections require prompt oral/periodontal care.
- If periodontitis is diagnosed, it should be managed without delay. immediately.
- Irrespective of the level of diabetes control, non-surgical periodontal therapy should be provided, as this may help to improve glycaemic control.
- Surgical periodontal and implant therapy is not indicated in patients who do not have acceptable diabetes control. In well-controlled patients, the results of surgical interventions are equivalent to patients without diabetes. However, attention should be paid to:

- people with poorly controlled diabetes, who have an increased risk of post-operative infections;
- patients managed with insulin or sulfonylureas, when the physician should be consulted about the timing of the planned procedure and a possible change in dosage of therapy to reduce the risk of intraoperative hypoglycaemia;
- People with diabetes who have extensive tooth loss should be encouraged to pursue dental rehabilitation to restore adequate mastication for proper nutrition.
- People with diabetes should also be evaluated for other potential oral complications, including dry mouth, burning mouth, candida infections and dental caries.
- For children and adolescents diagnosed with diabetes, an annual oral screening for early signs of periodontal involvement and dental caries is recommended starting as early as possible.
- Patients who present in the dental surgery/office without a diagnosis of diabetes, but with risk factors for type 2 diabetes should be informed about their risk for having diabetes and referred to a physician for appropriate diagnostic testing and follow-up care.
 - Patients risk may be screened for using a validated questionnaire. For example, in a Causcasian population (FindRisk Questionnaire - http://www.idf.org/webdata/docs/FINDRISC_English.pdf) – appendix 1
 - For oral health professionals with a special interest in diabetes, they may wish to consider screening based upon the recommendations of the American Diabetes Association (Diabetes Care 2017) – appendix 2

- If symptomatic (polydipsia, polyuria, polyphagia, unexplained weight loss), refer directly to a physician.

Guidelines for patients at the dental surgery/office who have diabetes or are found to be at risk for diabetes

- People with diabetes have a higher chance of getting gum disease.
- You may think that you are doing well managing your gum health, but you may not be doing enough because you have an increased risk of gum problems.
- Like diabetes, gum disease is a chronic condition and requires lifelong maintenance.
- You also need to clean your teeth and gums very carefully at home. Personalised advice will be provided by your oral health professional. This may include:
 - twice daily brushing with either manual or electric toothbrush
 - cleaning between your teeth using interdental brushes where they fit; where they do not fit, then flossing may be useful
 - the use of specific dentifrices and/or mouth rinses with proven activity against dental plaque, if advised by oral health professionals.
- If left untreated, gum disease can lead to tooth loss and may also make your diabetes harder to control.
- Gum disease may be present and get worse with no apparent symptoms to you, so if your dentist told you that you do not have gum disease now, you should still get regular dental check-ups as part of managing your diabetes. Your dentist will be able to pick up early signs of gum disease.
- You may have gum disease if you have ever noticed:
 - Red or swollen gums;

- Bleeding from your gums or blood in the sink after you brush your teeth;
 - Foul taste;
 - Longer looking teeth;
 - Loose teeth;
 - Increasing spaces between your teeth;
 - Calculus (tartar) on your teeth.
- People with diabetes may also suffer from dry mouth, burning mouth, yeast infections of the mouth or poor healing of mouth wounds.
- Remember to inform your dentist about the outcome of your visits to your doctor and provide an update of the results of your diabetes control and changes in medications.
- It is important to keep your mouth and your whole body as healthy as possible with regular dental and medical care.

References:

Allen, E. M., Matthews, J. B., DJ, O. H., Griffiths, H. R. & Chapple, I. L. (2011) Oxidative and inflammatory status in Type 2 diabetes patients with periodontitis. *Journal of Clinical Periodontology* **38**, 894–901.

Al-Harhi, L.S., Cullinan, M.P., Leichter, J.W., Thomason, W.M. (2013) The impact of periodontitis on oral health-related quality of life: a review of the evidence from observational studies. *Australian Dental Journal* **58**, 274-277.

Albert, D.A., Ward, A., Allweis. P., Graves, D.T., Knowler, W.C., Kunzel, C., Leibel, R.L., Novak, K.F., Oates, T.W., Papapanou, P.P., Schmidt, A.M., Taylor, G.W., Lamster, I.B., Borgnakke, W. S., Ylostalo, P. V., Taylor, G. W. & Genco, R. J. (2013) Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence. *Journal of Clinical Periodontology* **40** (Suppl 14), 135–152.

Buset, S.L., Walter, C., Friedmann, A., Weiger, R., Borgnakke, W.S., Zitzmann, N.U. (2016) Are periodontal diseases really silent? A systematic review of their effect on quality of life. *Journal of Clinical Periodontology* **43**, 333-344.

Chapple, I.L.C., Genco, R. (2013) Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Clinical Periodontology* **40** (s14), 106-112.

Cianciola, L., Park, B., Bruck, E., Mosovich, L., Genco, R. (1982) Prevalence of periodontal disease in insulin-dependent diabetes mellitus (juvenile diabetes). *Journal of the American Dental Association* **104**, 653-60.

Classification and Diagnosis of Diabetes (2017). *Diabetes Care* **40**, (Suppl 1), S14.

Demmer, R. T., Jacobs, D. R. Jr & Desvarieux, M. (2008) Periodontal disease and incident type 2 diabetes: results from the First National Health and Nutrition Examination Survey and its epidemiologic follow-up study. *Diabetes Care* **31**, 1373–1379.

Emrich LJ, Shlossman M, Genco RJ. (1991) Periodontal disease in non-insulin dependent diabetes mellitus. *Journal of Periodontology* **62**, 123-31.

Eke, P. I., Wei, L., Thornton-Evans, G. O., Borrell, L. N., Borgnakke, W. S., Dye, B. & Genco, R. J. (2016) Risk Indicators for Periodontitis in US Adults: NHANES 2009 to 2012. *Journal of Periodontology* **87**, 1174-1185.

Engelbreton, S. & Kocher, T. (2013) Evidence that periodontal treatment improves diabetes outcomes: a Systematic Review and Meta-analysis. *Journal of Clinical Periodontology* **40** (Suppl 14), 153–163.

Garcia, R. I., Krall, E. A. & Vokonas, P. S. (1998) Periodontal disease and mortality from all causes in the VA Dental Longitudinal Study. *Annals of Periodontology/the American Academy of Periodontology* **3**, 339–349.

Graziani, P., Gennal, S., Solini, A. & Petrini, M. (2017) A systematic review and meta-analysis of epidemiologic observational evidence on the effect of periodontal disease on diabetes: an update of the review of the EFP-AAP workshop. *Journal of Clinical Periodontology* **44**, submitted for publication.

International Diabetes Federation. IDF Diabetes Atlas (2015), 7th edn. Brussels, Belgium: International Diabetes Federation. <http://www.diabetesatlas.org>

Jepsen, S., J. Blanco, W. Buchalla, J. C. Carvalho, T. Dietrich, C. Dorfer, K. A. Eaton, E. Figuero, J. E. Frencken, F. Graziani, S. M. Higham, T. Kocher, M. Maltz, A. Ortiz-Vigon,

J. Schmoekel, A. Sculean, L. M. Tenuta, M. H. van der Veen, and V. Machiulskiene. (2017). 'Prevention and control of dental caries and periodontal diseases at individual and population level: consensus report of group 3 of joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases', *J Clin Periodontol*, **44** Suppl 18: S85-S93.

Kassebaum, N. J., Bernabe, E., Dahiya, M., Bhandari, B., Murray, C. J. & Marcenes, W. (2014) Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. *Journal of Dental Research* **93**, 1045-1053.

Kassebaum, N. J., Bernabe, E., Dahiya, M., Bhandari, B., Murray, C. J. & Marcenes, W. (2015) Global burden of untreated caries: a systematic review and metaregression. *Journal of Dental Research* **94**, 650-658.

Lalla, E. (2012) Diabetes and oral disease: implications for health professionals *Annals New York Academy of Sciences* **1255**, 1-15.

Lalla, E., Cheng, B., Lal, S., Tucker, S., Greenberg, E., Goland, R., Lamster, I.B. (2006) Periodontal changes in children and adolescents with diabetes: a case-control study. *Diabetes Care* **29**, 295-299.

Linden, G. J., Linden, K., Yarnell, J., Evans, A., Kee, F. & Patterson, C. C. (2012) All-cause mortality and periodontitis in 60–70-year-old men: a prospective cohort study. *Journal of Clinical Periodontology* **39**, 940–946.

Lindstrom, J., Tuomilehto, J. (2003) The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care* **26**: 725–731

Madianos PN. & Koromantzios PA. (2017) An update of the evidence on the potential impact of periodontal therapy on diabetes outcomes. *Journal of Clinical Periodontology* **44**,

submitted for publication.

Mealey BL. Periodontal disease and diabetes. A two-way street. (2006) *Journal of the American Dental Association* **137** Suppl:26S–31S

Meyle, J., Chapple, I. (2015) Molecular aspects of the pathogenesis of periodontitis. *Periodontology 2000*, **69**, 7–17.

Morita, I., Inagaki, K., Nakamura, F., Noguchi, T., Matsubara, T., Yoshii, S., Nakagaki, H., Mizuno, K., Sheiham, A. & Sabbah, W. (2012) Relationship between periodontal status and levels of glycated hemoglobin. *Journal of Dental Research* **91**, 161–166.

Polak, D. & Shapira, L. (2017) An update of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. *Journal of Clinical Periodontology* **44**, *submitted for publication.*

Saito, T., Shimazaki, Y., Kiyohara, Y., Kato, I., Kubo, M., Iida, M. & Koga, T. (2004) The severity of periodontal disease is associated with the development of glucose intolerance in non-diabetics: the Hisayama study. *Journal of Dental Research* **83**, 485–490.

Sanz, M., Kornman, K. (2013) Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Clinical Periodontology* **40** (s14), 164-169.

Sharma, P., Dietrich, T., Ferro, C.J., Cockwell, P., Chapple, I.L.C. (2016), Association between Periodontitis and mortality in stages 3-5 Chronic Kidney Disease: NHANES III and linked mortality study. *Journal of Clinical Periodontology* **43**, 104-113.

Söder, B., Jin, L.J., Klinge, B., Söder, P.-Ö. (2015) Periodontitis and premature death: a 16-year longitudinal study in a Swedish urban population. *Journal of Periodontal Research* **42**, 361-366.

Soikkonen, K., Wolf, J., Salo, T., Tilvis, R. (2000) Radiographic periodontal attachment loss as an indicator of death risk in the elderly. *Journal of Clinical Periodontology* **27**, 87-92.

Taylor, G.W., Burt, B.A., Becker, M.P., Genco, R.J. Shlossman, M., Knowler, W.C., Pettitt, D.J. (1998) Non-insulin dependent diabetes mellitus and alveolar bone loss progression over 2 years. *Journal of Periodontology* **69**, 76-83.

Taylor GW. (2001) Bidirectional interrelationships between diabetes and periodontal diseases: an epidemiologic perspective. *Annals of Periodontology* **6**, 99-112

Tonetti, M.S., VanDyke, T.E. (2013) Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *Journal of Clinical Periodontology* **40** (s14), 24-29.

White, D.A., Tsakos, G., Pitts, N.B., Fuller E, Douglas GV, Murray JJ, Steele JG. (2012). Adult Dental Health Survey 2009: common oral health conditions and their impact on the population. *British dental Journal* **213**, 567-572.

Appendix 1: FindRisk Questionnaire (Lindstrom & Tuomilehto 2003)

TYPE 2 DIABETES RISK ASSESSMENT FORM

Circle the right alternative and add up your points.

1. Age

- 0 p. Under 45 years
- 2 p. 45–54 years
- 3 p. 55–64 years
- 4 p. Over 64 years

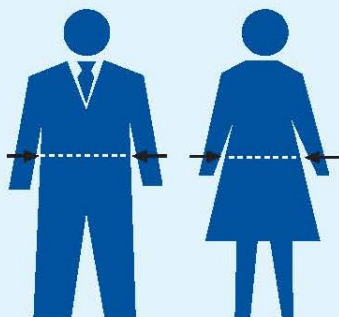
2. Body-mass index

(See reverse of form)

- 0 p. Lower than 25 kg/m²
- 1 p. 25–30 kg/m²
- 3 p. Higher than 30 kg/m²

3. Waist circumference measured below the ribs (usually at the level of the navel)

- | | MEN | WOMEN |
|------|------------------|-----------------|
| 0 p. | Less than 94 cm | Less than 80 cm |
| 3 p. | 94–102 cm | 80–88 cm |
| 4 p. | More than 102 cm | More than 88 cm |



4. Do you usually have daily at least 30 minutes of physical activity at work and/or during leisure time (including normal daily activity)?

- 0 p. Yes
- 2 p. No

5. How often do you eat vegetables, fruit or berries?

- 0 p. Every day
- 1 p. Not every day

6. Have you ever taken medication for high blood pressure on regular basis?

- 0 p. No
- 2 p. Yes

7. Have you ever been found to have high blood glucose (eg in a health examination, during an illness, during pregnancy)?

- 0 p. No
- 5 p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?

- 0 p. No
- 3 p. Yes: grandparent, aunt, uncle or first cousin (but no own parent, brother, sister or child)
- 5 p. Yes: parent, brother, sister or own child

Total Risk Score

The risk of developing type 2 diabetes within 10 years is

- | | |
|-----------------------|--|
| Lower than 7 | Low: estimated 1 in 100 will develop disease |
| 7–11 | Slightly elevated: estimated 1 in 25 will develop disease |
| 12–14 | Moderate: estimated 1 in 6 will develop disease |
| 15–20 | High: estimated 1 in 3 will develop disease |
| Higher than 20 | Very high: estimated 1 in 2 will develop disease |

Please turn over

WHAT CAN YOU DO TO LOWER YOUR RISK OF DEVELOPING TYPE 2 DIABETES?

You can't do anything about your age or your genetic predisposition. On the other hand, the rest of the factors predisposing to diabetes, such as overweightness, abdominal obesity, sedentary lifestyle, eating habits and smoking, are up to you. Your lifestyle choices can completely prevent type 2 diabetes or at least delay its onset until a much greater age.

If there is diabetes in your family, you should be careful not to put on weight over the years. Growth of the waistline, in particular, increases the risk of diabetes, whereas regular moderate physical activity will lower the risk. You should also pay attention to your diet: take care to eat plenty of fibre-rich cereal products and vegetables every day. Omit excess hard fats from your diet and favour soft vegetable fats.

Early stages of type 2 diabetes seldom cause any symptoms. If you scored 12–14 points in the Risk Test, you would be well advised to seriously consider your physical activity and eating habits and pay attention to your weight, to prevent yourself from developing diabetes. Please contact a public-health nurse or your own doctor for further guidance and tests.

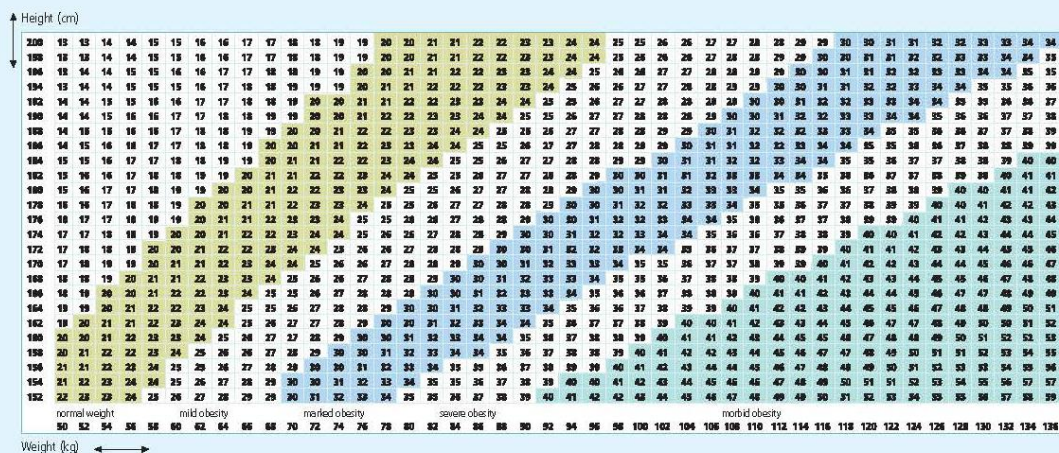
If you scored 15 points or more in the Risk Test, you should have your blood glucose measured (both fasting value and value after a dose of glucose or a meal) to determine if you have diabetes without symptoms.

BODY-MASS INDEX

The body-mass index is used to assess whether a person is normal weight or not. The index is calculated by dividing body weight (kg) by the square of body height (m). For example, if your height is 165 cm and your weight 70 kg, your body-mass index will be $70/(1.65 \times 1.65)$, or 25.7.

If your body-mass index is 25–30, you will benefit from losing weight; at least you should take care that your weight doesn't increase beyond this. If your body-mass index is higher than 30, the adverse health effects of obesity will start to show, and it will be essential to lose weight.

BODY-MASS INDEX CHART



Appendix 2: Criteria for Screening according to the recommendations of the American Diabetes Association (Diabetes Care 2017)

Table 1 – Criteria for testing for diabetes or prediabetes in asymptomatic adults
From Diabetes Care 2017.

1. Testing should be considered in overweight or obese ($\text{BMI} \geq 25 \text{ kg/m}^2$ or $\geq 23 \text{ kg/m}^2$ in Asian American) adults who have one or more of the following risk factors:
 - $\text{A1C} \geq 5.7\%$ (39 mmol/mol), IGT, IFG on previous testing
 - First degree relative with diabetes
 - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
 - Women who were diagnosed with GDM
 - History of CVD
 - Hypertension ($\geq 140/90 \text{ mmHg}$ or on therapy for hypertension)
 - HDL cholesterol level $< 35 \text{ mg/dL}$ and/or a triglyceride level $> 250 \text{ mg/dL}$ (2.82 mmol/L)
 - Women with polycystic ovary syndrome
 - Physical inactivity
 - Other clinical conditions associated with insulin resistance (eg severe obesity, acanthosis nigricans).
2. For all patients, disease testing should begin at age 45 years
3. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results (e.g, those with prediabetes should be tested yearly) and risk status.